General

Guideline Title

Clinical policy: use of intravenous tissue plasminogen activator for the management of acute ischemic stroke in the emergency department.

Bibliographic Source(s)

Brown MD, Burton JH, Nazarian DJ, Promes SB, American College of Emergency Physicians. Clinical policy: use of intravenous tissue plasminogen activatorÂ for the management of acute ischemic stroke in the emergency department. Ann Emerg Med. 2015 Sep;66(3):322-333.e31. [100 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Edlow JA, Smith EE, Stead LG, Gronseth G, Messe SR, Jagoda AS, Wears RL, Decker WW, American College of Emergency Physicians, American Academy of Neurology. Clinical policy: use of intravenous tPA for the management of acute ischemic stroke in the emergency department. Ann Emerg Med. 2013 Feb;61(2):225-43. [46 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions for the strength of evidence (Class I-III) and strength of recommendations (Level A-C) are provided at the end of the "Major Recommendations" field.

1. Is intravenous tissue plasminogen activator (IV tPA) safe and effective for patients with acute ischemic stroke if given within 3 hours of symptom onset?
   Level A recommendations. None specified.

   Level B recommendations. With a goal to improve functional outcomes, IV tPA should be offered and may be given to selected patients with acute ischemic stroke within 3 hours after symptom onset at institutions where systems are in place to safely administer the medication. The increased risk of symptomatic intracerebral hemorrhage (sICH) should be considered when deciding whether to administer IV tPA to patients with acute ischemic stroke.

   Level C recommendations. When feasible, shared decisionmaking between the patient (and/or his or her surrogate) and a member of the health care team should include a discussion of potential benefits and harms prior to the decision whether to administer IV tPA for acute ischemic stroke. (Consensus recommendation).

2. Is IV tPA safe and effective for patients with acute ischemic stroke treated between 3 to 4.5 hours after symptom onset?
   Level A recommendations. None specified.

   Level B recommendations. Despite the known risk of sICH and the variability in the degree of benefit in functional outcomes, IV tPA may be offered and may be given to carefully selected patients with acute ischemic stroke within 3 to 4.5 hours after symptom onset at institutions where systems are in place to safely administer the medication.

   Level C recommendations. When feasible, shared decision making between the patient (and/or his or her surrogate) and a member of the health care team should include a discussion of potential benefits and harms prior to the decision whether to administer IV tPA for acute ischemic stroke. (Consensus recommendation)

Definitions

Strength of Evidence

*Literature Classification Schema**

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)

*Some designs (e.g., surveys) will not fit this schema and should be assessed individually.

†Objective is to measure therapeutic efficacy comparing interventions.

‡Objective is to determine the sensitivity and specificity of diagnostic tests.

§Objective is to predict outcome including mortality and morbidity.

*Approach to Downgrading Strength of Evidence**

Downgrading	Design/Class		
	1	2	3
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

*See the "Description of Methods Used to Analyze the Evidence" field for more information.

Strength of Recommendations

Strength of recommendations regarding each critical question were made by subcommittee members using results from strength of evidence grading, expert opinion, and consensus among subcommittee members according to the following guidelines:

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of clinical certainty (i.e., based on evidence from 1 or more Class of Evidence I or multiple Class of Evidence II studies).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reï¬,ect moderate clinical certainty (i.e., based on evidence from 1 or more Class of Evidence II studies or strong consensus of Class of Evidence III studies).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of any adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, and publication bias, among others, might lead to such a downgrading of recommendations.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Acute ischemic stroke

Guideline Category

Assessment of Therapeutic Effectiveness

Management

Treatment

Clinical Specialty

Emergency Medicine

Neurology

Intended Users

Physicians

Guideline Objective(s)

To derive evidence-based recommendations to help clinicians answer the following critical questions:

- Is intravenous tissue plasminogen activator (IV tPA) safe and effective for patients with acute ischemic stroke if given within 3 hours of symptom onset?
- Is IV tPA safe and effective for patients with acute ischemic stroke treated between 3 to 4.5 hours after symptom onset?

Target Population

Adult patients aged 18 years and older presenting to the emergency department with acute ischemic stroke

Note: This guideline is not intended to be used for pediatric or pregnant patients.

Interventions and Practices Considered

1. Intravenous tissue plasminogen activator (IV tPA) administered within 3 to 4.5 hours of symptom onset
2. Shared decision making between the patient (and/or his or her surrogate) and a member of the health care team

Major Outcomes Considered

- Incidence of symptomatic intracerebral hemorrhage (sICH)
- Functional outcomes (as measured by modified Rankin Scale scores)
- Mortality rates

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

This clinical policy was created after careful review and critical analyses of the medical literature and was based on a systematic review of the literature. Searches of MEDLINE, MEDLINE InProcess and other nonindexed citations portion of MEDLINE, and the Cochrane Database were performed. All searches were limited to English-language sources, human studies, and adults, from January 2011 to September 2014; searches were conducted on January 27, 2014, and September 3, 2014. Specific key words/phrases and inclusion criteria used in the searches are identified in the original guideline document under each critical question.

Relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were also included.

Number of Source Documents

Study Selection

1,765 references were identified in the updated literature search as potentially relevant to the critical questions (992 in the search on January 27, 2014, and 773 in the search on September 3, 2014). From these, 136 articles were selected from the January 27, 2014 search, and 59 articles from the September 3, 2014 search, resulting in a total of 195 new articles for full-text review.

For this policy, recommendations for question 1 were based on 1 Class I randomized controlled trial, 5 Class II articles, and 29 Class III studies. For question 2, recommendations were based on 1 Class II randomized controlled trial and 42 Class III studies.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Strength of Evidence

Literature Classification Schema*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)

*Some designs (e.g., surveys) will not fit this schema and should be assessed individually.

†Objective is to measure therapeutic efficacy comparing interventions.

‡Objective is to determine the sensitivity and specificity of diagnostic tests.

§Objective is to predict outcome including mortality and morbidity.

Approach to Downgrading Strength of Evidence*

Downgrading	Design/Class		
	1	2	3
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

*See the "Description of Methods Used to Analyze the Evidence" field for more information.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Assessment of Classes of Evidence

All articles used in the formulation of this clinical policy were graded by at least 2 committee members or methodologists; all Class I and Class II articles were graded by at least 2 methodologists. Each article was assigned a design class with design 1 representing the strongest study design and subsequent design classes (e.g., design 2, design 3) representing respectively weaker study designs for therapeutic, diagnostic, or prognostic clinical reports, or meta-analyses (see the "Rating Scheme for the Strength of the Evidence" field). Articles were then graded on dimensions related to the study's methodological features, such as randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassi¯cation biases, sample size, and generalizability. Using a predetermined process related to

the study's design, methodological quality, and applicability to the critical question, articles received a ï¬nal Class of Evidence grade (i.e., Class I, Class II, Class III, or Class X) (see the "Rating Scheme for the Strength of the Evidence" field). Articles identiï¬ed with fatal ï¬,aws or that were ultimately not applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating recommendations for this policy. Grading was done with respect to the speciï¬c critical questions; thus, the level of evidence for any one study may vary according to the question for which it is being considered. As such, it was possible for a single article to receive different Classes of Evidence as different critical questions were answered from the same study. Question-speciï¬c Classes of Evidence grading can be found in the Evidentiary Table in the original guideline document.

Additionally, given recent changes to the American College of Emergency Physicians (ACEP) clinical policy development process, articles rated as Class I or II in the 2012 policy were also reviewed and graded by the committee methodologists using current grading forms (available at http://acep.org/clinicalpolicies).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

This policy is a product of the American College of Emergency Physicians (ACEP) clinical policy development process and is based on the existing literature; when literature was not available, consensus of emergency physicians was used.

When possible, clinically oriented statistics (e.g., likelihood ratios, number needed to treat [NNT]) are presented to help the reader better understand how the results may be applied to the individual patient. For a definition of these statistical concepts, see Appendix C in the original guideline document.

Rating Scheme for the Strength of the Recommendations

Strength of recommendations regarding each critical question were made by subcommittee members using results from strength of evidence grading, expert opinion, and consensus among subcommittee members according to the following guidelines:

Strength of Recommendations

Level A recommendations. Generally accepted principles for patient care that reï¬,ect a high degree of clinical certainty (i.e., based on evidence from 1 or more Class of Evidence I or multiple Class of Evidence II studies).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reï¬,ect moderate clinical certainty (i.e., based on evidence from 1 or more Class of Evidence II studies or strong consensus of Class of Evidence III studies).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of any adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, and publication bias, among others, might lead to such a downgrading of recommendations.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

This clinical policy was approved by the American College of Emergency Physicians (ACEP) Board of Directors on June 24, 2015.

This guideline was endorsed by the Emergency Nurses Association on July 14, 2015.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

For this policy, recommendations for question 1 were based on 1 Class I randomized controlled trial, 5 Class II articles, and 29 Class III studies. For question 2, recommendations were based on 1 Class II randomized controlled trial and 42 Class III studies.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

See the "Potential Benefits" sections in the original guideline document for information on benefits of the specific interventions.

Potential Harms

See the "Potential Harms" sections in the original guideline document for information on harms of the specific interventions.

Qualifying Statements

Qualifying Statements

- Policy statements and clinical policies are the official policies of the American College of Emergency Physicians (ACEP) and, as such, are not subject to the same peer review process as articles appearing in the print journal. Policy statements and clinical policies of ACEP do not necessarily reflect the policies and beliefs of *Annals of Emergency Medicine* and its editors.
- This policy is not intended to be a complete manual on the evaluation and management of patients with acute ischemic stroke but rather a focused examination of critical issues that have particular relevance to the current practice of emergency medicine.
- It is the goal of the Clinical Policies Committee to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain adequate empirical data to answer a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.
- This clinical policy is not intended to represent a legal standard of care for emergency physicians. Recommendations offered in this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP recognizes the importance of the individual physician's judgment and patient preferences. This guideline deï¬nes for the physician those strategies for which medical literature exists to provide support for answers to the critical questions addressed in this policy.

Implementation of the Guideline

Description of Implementation Strategy

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Safety

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Feb (revised 2015 Sep)

Guideline Developer(s)

American College of Emergency Physicians - Medical Specialty Society

Source(s) of Funding

American College of Emergency Physicians (ACEP)

Guideline Committee

American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Use of Intravenous tPA for Ischemic Stroke

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Financial Disclosures/Conflicts of Interest

Relevant industry relationships: There were no relevant industry relationships disclosed by the subcommittee members.

Relevant industry relationships are those relationships with companies associated with products or services that signi¯cantly impact the speci¯c aspect of disease addressed in the critical question.

Guideline Endorser(s)

Emergency Nurses Association - Professional Association

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Edlow JA, Smith EE, Stead LG, Gronseth G, Messe SR, Jagoda AS, Wears RL, Decker WW, American College of Emergency Physicians, American Academy of Neurology. Clinical policy: use of intravenous tPA for the management of acute ischemic stroke in the emergency department. Ann Emerg Med. 2013 Feb;61(2):225-43. [46 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Emergency Physicians (ACEP) Web site .

A summary of this guideline optimized for mobile viewing is available under the CQ tab at the ACEP Web site .

Availability of Companion Documents

The following are available:

- American College of Emergency Physicians clinical policy development. 3 p. Available from the American College of Emergency Physicians (ACEP) Web site .
- ACEP clinical policy development process. Flow chart. 1 p. Available from the ACEP Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on March 29, 2013. The information was verified by the guideline developer on May 2, 2013. This summary was updated by ECRI Institute on October 28, 2015. The updated information was verified by the guideline developer on November 17, 2015.

Copyright Statement

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